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Carriage of methicillin-resistant *Staphylococcus aureus* on admission to European rehabilitation centres—a prospective study

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Abstract

This study aimed to determine the prevalence of and risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) carriage among patients newly admitted to rehabilitation centres. It is a prospective study examining MRSA carriage on admission to seven rehabilitation wards in four countries. Risk factors for MRSA carriage were analysed using univariate and multivariate analyses. A total of 1204 patients were studied. Among them, 105 (8.7%) had a positive admission MRSA screening result. The MRSA carriers were more likely to be male, to have had a recent stay in another long-term-care facility or >2 weeks acute-care hospital stay, history of colonization with MRSA, reduced level of consciousness, peripheral vascular disease and pressure sores. In multivariable logistic regression male gender (odds ratio (OR) 2.2, 95% confidence interval (CI) 1.4–3.6, p 0.001), history of MRSA positivity (OR 6.8, 95% CI 3.8–12.3, p <0.001), peripheral vascular disease (OR 2.5, 95% CI 1.2–5, p 0.013), recent stay in another long-term-care facility (OR 2.1, 95% CI 1.3–3.5, p 0.004), or long (>2 weeks) acute-care hospital stay (OR 1.9, 95% CI 1.2–3, p 0.004), remained significant risk factors for MRSA carriage. MRSA carriage is common on admission to rehabilitation centres but less so, than previously described in long-term-care facilities. Male gender, history of MRSA positivity, previous hospitalization and peripheral vascular disease may predict MRSA carriage, and may serve as indicators for using pre-emptive infection control measures.

Keywords: Long-term-care, methicillin-resistant *Staphylococcus aureus*, rehabilitation
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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) was first described in the early 1960s, and since then these strains have spread in acute-care hospitals worldwide causing a variety of clinical syndromes ranging in severity from simple to life-threatening infections [1,2].

Although data regarding MRSA carriage in acute-care hospitals are widely available, firm data regarding facilities for long-term care, including rehabilitation centres, are sparse.

The amount of care provided in long-term-care facilities (LTCFs) has dramatically increased in the last decade, making the question of MRSA carriage in this setting important but unanswered. Patient exchange between rehabilitation centres and acute-care hospitals is common, so reciprocal effects exist between these institutions, and LTCFs are being increasingly recognized as having a pivotal role in the spread of antibiotic resistance [3,4].

The LTCFs are heterogeneous, ranging from institutions that provide chronic care for the sick and elderly to rehabilitation centres, which are more dynamic and which provide

care to a large number of patients with different needs. Patients in rehabilitation centres have multiple characteristics that are often found among MRSA carriers; most patients are admitted after a long and complicated hospital stay, they often have suffered multiple trauma, may have invasive devices, and in some cases have been treated with multiple antibiotic agents [3,4]. Moreover, host-related factors such as older age, poor functional status, mental impairment, alterations in mobility or swallowing and urinary incontinence, are especially associated with higher risk of developing infections [3,4].

High rates of MRSA carriage have been found in LTCFs, ranging between 8.8% and 23% [5–11]. However, most of these were single-centre studies [5–7,9–11] and were performed in LTCFs other than rehabilitation centres (nursing homes or veteran centres) [5–9]. Moreover, these were point prevalence studies, and do not provide information on carriage upon admission to these facilities [5–9].

Hence, the aim of the present study was to determine the prevalence of and risk factors for MRSA carriage in a large number of patients newly admitted to seven rehabilitation wards in four different countries.

Methods

Settings

This study is part of the Mastering Hospital Antimicrobial Resistance in Europe (MOSAR) study, a European Commission-funded trans-disciplinary network devoted to the combat and control of antimicrobial resistance in bacteria. The project focuses on endemic and epidemic nosocomial pathogens in high-risk medical units including intensive-care units, and surgery and rehabilitation centres in countries with high levels of resistance. Here we present a portion of the results from MOSAR work package 5, examining resistance in rehabilitation centres.

The study was conducted at seven wards in four rehabilitation centres: Tel-Aviv, Israel (two geriatric rehabilitation wards); Badalona, Spain, (a spinal cord injury rehabilitation unit); Rome, Italy, (one neurological and one orthopaedic rehabilitation unit); and Berck, France, (two neurological and orthopaedic rehabilitation wards).

These wards have a total of 290 hospital beds: 203 for neurological rehabilitation, 34 for orthopaedic rehabilitation and one ward of 53 beds dedicated to both. The study included adult patients newly admitted to the study wards between October 2008 and March 2010 (for 10–12 months in each centre).

Design

This was a prospective case–control study, examining risk factors for carriage of MRSA on admission to a rehabilitation centre. Cases were newly admitted patients who were found to be MRSA carriers when screened upon admission, and controls were those who were MRSA negative upon screening. Cultures were taken on admission from all patients newly admitted to the rehabilitation wards during the study period.

Data collection

For purposes of the study, the following data were recorded: demographics—patient age and sex, medical history including underlying conditions, previous hospital or other LTCF stay, previous history of colonization or infection with MRSA, history of antibiotic treatment during the month before admission, comorbidities, dependence in activities of daily living, cognitive function and the presence of medical devices.

Microbiological methods

To assess MRSA colonization, samples for MRSA culture were obtained from all newly admitted patients within 24 h of admission. A nasal swab (Copan Italia, Brescia, Italy) was taken from the anterior nares of each patient. Microbiological methods used were evaluated as previously described [12]; briefly, swabs were transferred to the laboratory and were directly plated onto BBL CHROMagar MRSA II medium (BD Diagnostics, Sparks, MD, USA). Plates were kept and handled according to the manufacturer's instructions. After incubation for 24 h, plates were read. Suspected MRSA colonization was recorded for samples from which mauve colonies were observed. Further verification for MRSA was obtained by colony morphology and size on tryptic soy broth 5% blood agar plates and by slide agglutination (Prolex, Staph Xtra Latex Kit; PRO-LAB Diagnostics, Richmond Hill, ON, Canada) in combination with DNase detection (DNase plates; Hy-Labs, Rehovot, Israel). Patients were recorded as MRSA non-carriers if mauve colonies were not observed after 24 h of incubation. All MRSA isolates recovered were identified according to a unique patient code and stored at −80°C for further investigation. Quality control testing was successfully performed on each lot of chromogenic medium using the MRSA ATCC 43300 and MSSA ATCC 29213 strains.

Statistical analysis

Risk factors were analysed by comparing MRSA-positive patients (cases) with MRSA-negative patients (controls). Data were analysed using univariate analysis: continuous variables

were compared between groups using an unpaired *t*-test within each group. Categorical parameters were compared by using the Pearson chi-square test and p values ≤0.05 were considered indicative of a significant difference between groups. Multivariate analysis using logistic regression prediction models was constructed using forward stepwise (P to enter = 0.1, P to remain = 0.05) selection. Interaction terms and confounding were examined. All data were analysed using SPSS software package version 15.0 (SPSS, Chicago, IL, USA).

Ethics

The study was approved by each local institutional ethics review board.

Results

A total of 1204 patients met the initial study criteria and were screened on admission. Among them 105 (8.7%) were positive for MRSA and 1099 (91.3%) were negative. The proportion of positive cultures on admission to the different rehabilitation centres was as follows: France 14.6%, Spain 8.1%, Italy 7.3% and Israel 7.1%. The proportion of positive cultures was significantly higher in the French centre than in the other three centres (p <0.001, OR 2.2; 95% CI 1.4–3.4). There was no significant difference in the proportion of positive MRSA screening results between the patients admitted for neurological or orthopaedic rehabilitation (8.7% versus 6.7%, respectively, p 0.26).

Table 1 summarizes the characteristics and comorbidities of the patients according to their MRSA carriage status at admission. Patients with positive results were more likely to be male, to have had a recent stay in another LTCF or a long (>2 weeks) acute-care hospital stay and a history of colonization with MRSA.

Comorbidities and conditions that were found to be significantly more common in the MRSA group included reduced level of consciousness at the time of admission as well as peripheral vascular disease and pressure sores. Antibiotic treatment in the month before admission was not associated with MRSA status on admission.

Variables that were significantly different between the groups were entered into the multivariable logistic regression model. In this model, male gender, history of colonization with MRSA, peripheral vascular disease, recent stay in another LTCF or long (>2 weeks) acute-care hospital stay were found to be independently associated with MRSA screening positivity on admission (Table 2). Centre effect was examined by including it as a variable in the model and was not found to be significantly associated with MRSA status on admission or to affect the model significantly.

Although history of colonization with MRSA in the past was found to be the strongest predictor for having a positive MRSA screening result in a multivariable logistic regression model (OR 6.8, Table 2), most patients with a past history

TABLE 1. Comparison of demographic characteristics and comorbidities in patients with positive and negative results on methicillin-resistant *Staphylococcus aureus* screening

	MRSA positive (*n* = 105)	MRSA negative (*n* = 1099)	p	OR
Demographic parameters				
Male: female (%)	69/31	45/55	<0.001	4
Age mean ± SD (year)	68.3 ± 19.8	69.3 ± 18.6	0.6	
Age >65 years (*n*, %)	60 (57.1)	734 (66.8)	0.041	0.6
Admitted from acute-care facility (*n*, %)	91 (86.7)	955 (86.9)	0.99	1
Long acute-care hospital stay (>2 weeks) (*n*, %)	66 (62.9)	464 (42.2)	<0.001	2.3
Recent stay in another long-term-care facility (*n*, %)	46 (43.8)	271 (24.7)	<0.001	2.4
Comorbidities				
History of colonization with MRSA (*n*, %)	28 (26.7)	45 (4.1)	<0.001	8.5
History of colonization with multidrug resistance bacteria other than MRSA (*n*, %)	1 (1)	31 (2.8)	0.4	0.4
Admitted with infection	11 (10.5)	126 (11.5)	0.76	0.9
Reduced level of consciousness (*n*, %)	25 (23.8)	152 (13.8)	0.006	1.9
Cardiovascular disease (*n*, %)	60 (57.1)	654 (59.5)	0.58	0.9
Peripheral vascular disease (*n*, %)	13 (12.4)	52 (4.7)	0.001	2.8
Pressure sores (*n*, %)	20 (19)	98 (8.9)	0.001	2.4
Diabetes mellitus (*n*, %)	24 (22.9)	237 (22)	0.78	1.1
Chronic lung disease (*n*, %)	14 (13.3)	99 (9)	0.15	1.5
Cerebral vascular accident/transient ischaemic attack (*n*, %)	20 (19)	171 (16)	0.36	1.3
Tetraplegia/Quadriplegia (*n*, %)	20 (19)	141 (12.8)	0.07	1.6
Dementia (*n*, %)	6 (5.7)	70 (6.4)	0.78	0.9
Renal disease (*n*, %)	16 (15.2)	106 (9.6)	0.07	1.7
Malignancy (*n*, %)	10 (9.5)	175 (15.9)	0.08	0.6
Immunodeficiency (*n*, %)	9 (8.6)	49 (4.5)	0.06	2
Surgery/Invasive procedure in last year (*n*, %)	72 (68.6)	665 (60.5)	0.12	1.4
Invasive device in the past month (*n*, %)	78 (74.3)	764 (69.5)	0.38	1.2

MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio.

TABLE 2. Multivariable logistic regression model demonstrating variables associated with methicillin-resistant *Staphylococcus aureus* colonization

	OR	95% CI	p
Gender (male)	2.2	1.4–3.6	0.001
History of colonization with MRSA	6.8	3.8–12.3	<0.001
Peripheral vascular disease	2.5	1.2–5	0.013
Long acute-care hospital stay (>2 weeks)	1.9	1.2–3	0.004
Recent stay in another long-term-care facility	2.1	1.3–3.5	0.004

95% CI, 95% confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio.

of MRSA had a negative screening result on admission (45 of 73, 61.6%). To examine whether risk factors for MRSA positivity differed between patients without a history of MRSA carriage, we performed a subgroup analysis for patients who were not known to have been colonized with MRSA in the past (n = 1026). In this group of patients the predictors for positive MRSA screening were similar to those identified in the entire study cohort, including male gender (OR 2.6, 95% CI 1.5–4.3, p <0.001), peripheral vascular disease (OR 2.9, 95% CI 1.4–6.1, p 0.006), long (>2 weeks) acute-care hospital stay (OR 1.9, 95% CI 1.2–3.2, p 0.008) and recent stay in another LTCF (OR 1.7, 95% CI 0.99–2.8, p 0.054).

We also examined the subgroup of patients who were known to be colonized with MRSA in the past (n = 73). Patients admitted with infection and those receiving antibiotic treatment on admission were more likely to have negative screening results for MRSA than their counterparts (33% versus 11%, p 0.03, and 45% versus 14%, p 0.009, respectively). The types of infection in the subgroup of patients with a history of MRSA and a negative admission screen included urinary tract infection (n = 6), skin infection (n = 5), pneumonia (n = 2) and bacteraemia (n = 2).

Discussion

This multicentre, multinational large prospective study provides data on the prevalence of and risk factors for MRSA colonization on admission to rehabilitation centres. Our two main findings are a lower than expected MRSA colonization prevalence on admission and a description of the profile of MRSA carriers.

Previous studies were conducted in various types of LTCFs, and found the MRSA colonization prevalence to range from 8.8% to 23% [5–11]. In contrast, in this study we found a lower mean MRSA carriage prevalence of 8.7%, and in three of the four centres the prevalence was lower than the lowest previously reported. There are several possible explanations for this finding. First, our study was conducted in rehabilitation centres and most other studies were conducted in other types of LTCFs. Indeed, in previous reports from rehabilitation centres, prevalence was relatively low (12–16.5%) compared with other LTCFs, but it was still higher than the prevalence we found [9,10]. Second, a trend is presently observed in most European countries of decreasing rates of MRSA [13]. This decrease has been suggested to be related to the improved quality of infection control practices in medical centres, and to countrywide efforts to limit the spread of MRSA [13], as well as other factors. Interestingly, although according to the 2010 annual report of the European Antimicrobial Resistance Surveillance System (EARSS), France had a lower proportions of invasive MRSA infection compared with Italy and Spain (21.6% versus 36.5% and 25.3%, respectively), in our study the French centre had a higher MRSA carriage prevalence than the centres in Italy, Israel and Spain [13]. We believe that these variations in prevalence of MRSA colonization on admission to the four rehabilitation centres participating in the MOSAR study may reflect differences in prevalence of MRSA among referring centres as well as differences in patient populations referred to each of the centres [5–11]. Moreover, these variations may be related to differences between patient populations admitted to the four studied rehabilitation centres.

A third explanation for the lower than expected MRSA carriage prevalence in our study may relate to study design. Most previous studies in LTCFs were point prevalence studies, so most patients studied already had prolonged LTCF stay [5–9]; whereas our study included only newly admitted patients. This last explanation may have important ramifications: if indeed rates of MRSA carriage on admission to LTCFs are much lower than during a prolonged stay, then LTCFs are likely to be a significant hub for transmission and amplification of MRSA. This finding requires further confirmation from longitudinal studies analysing acquisition events, and if found correct, should be followed by interventions to reduce transmission.

The profile of MRSA carriers in our study reflects several domains. Risk for being a carrier on admission is higher with longer and more extensive contact with the healthcare setting (as reflected by longer stay in the acute-care setting and past stay in an LTCF). This finding has been described previously in multiple studies in various settings, and reflects the increased likelihood of MRSA acquisition in healthcare settings [6,8–10]. Another variable associated with a positive screening result on admission was a history of being an MRSA carrier. Indeed, carriage of MRSA may extend for periods of over 5 years, so even a remote history of MRSA

positivity should be considered a strong predictor, as found in our study. Interestingly, we found that 61.6% of those with a history of colonization had a negative screening result on admission. These patients had significantly higher rates of intercurrent infection on admission and treatment with an antibiotic (although mostly without MRSA coverage). This finding cannot be explained by direct activity of the antibiotic on suppressing MRSA, and may reflect an indirect effect on MRSA by changes in the nasopharyngeal microflora, which in turn may affect MRSA carriage. We believe that this finding deserves to be further studied. Male gender was found to be a risk factor, by us as well as in other studies [6,8]. Previous studies explained the male predominance among MRSA carriers by the fact that other risk factors for MRSA colonization are more prevalent among men than women [14].

The only comorbid condition found in our study to be associated with MRSA carriage was peripheral vascular disease. This association has not been described previously in the setting of LTCFs. We hypothesize that the association may reflect previous hospitalization in wards with a high prevalence of MRSA. In addition, the presence of non-intact skin as the result of peripheral vascular disease may promote colonization with MRSA.

Our study has several limitations. First, the rehabilitation wards that were studied are heterogeneous, representing various patient populations with differing indications for rehabilitation and different acute-care settings of origin. This variety may have reduced our ability to identify some important risk factors, which might have been detected had we studied a more homogeneous population. This limitation is offset by the greater generalizability deriving from studying a heterogeneous population. Second, our study used conventional culture not supplemented by molecular techniques to improve detection of MRSA carriage. This may have led to some misclassification of carriers as non-carriers. However, a recent study suggests that this misclassification may not occur frequently [15]. Moreover, if such misclassification did occur it would bias our results towards the null, thereby not diminishing the strength of our positive findings. Another potential limitation for our study regards the microbiological methods we used to detect MRSA carriers; first, only nasal swabs were screened while additional samples including throat, perineum and decubitus ulcers could potentially increase the sensitivity of the screening. Second, some authors suggest enrichment and prolonged incubation time of the screening agar to increase the recovery rate and raise the sensitivity of the screening. However, a recent study regarding this specific point did find excellent specificity of this more rapid method [16]. Nevertheless, we might have missed some newly admitted patients with very low colonization loads.

In summary, we found that MRSA colonization on admission to European rehabilitation centres is less common than expected. The discrepancy relative to the higher proportions of carriers found in previous point prevalence studies in LTCFs may reflect high intra-rehabilitation centre transmission and amplification of MRSA. We identified concurrent antibiotic treatment as a negative predictor of MRSA screen positivity among past carriers, which may suggest a reduction in the ability to detect carriage if screening is performed while receiving antibiotic treatment. As data regarding the specific consequences of MRSA colonization on patients in rehabilitation centres are lacking, and to better understand the epidemiology of MRSA in rehabilitation centres, further studies, including longitudinal studies, are required.

Transparency Declaration

We have nothing to declare.

Appendix

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